Amendments to the Specification:

Please replace the Title of the Application with the following new Title:

"METHOD FOR LIGAND DEVELOPMENT"

Please replace paragraph [0272] (page 70, line 16 to page 71, line 15) as follows:

[0272] A stock human α-thrombin solution (1.56 mg/mL) from Enzyme Research Labs was first diluted to 0.5 mg/mL (11 μM) with 50 mM Hepes, pH 7.5, 0.1 M NaCl (assay buffer, unless mentioned otherwise), and stored on ice. The five ligands (recrystallized solids characterized by mass spectrometry and NMR) were accurately weighed out to be 1.5 to 2.0 mg and dissolved in 1.0 mL of 100% DMSO so that the concentration was between 1.8 and 3.8 mM. A 96 well V-bottom Costar microplate was then set up such that 100 μL of the 11 μM human α-thrombin solution was pipetted into wells A1 through A6. This was followed by the addition of 2 μL of 3dp-3811 into well A2, 2 μL of 3dp-3959 into well A3, 2 μL of 3dp-4077 into well A4, 2 μL of 3dp-4076 into well A5, 2 μL of 3 dp-4026 into well A6, and 2 μL of 100% DMSO into control well A1. The contents were mixed by repeated uptake and discharge using a 100 μL pipette tip. Finally, one drop of mineral oil (Sigma, St. Louis, Mo.) was added on top of the wells to reduce evaporation of samples at elevated temperatures. The microplate was then placed on heating block 4 of ROBOCYCLER™ a RoboCycler Gradient 96 Temperature Cycler (Stratagene, La Jolla, Calif.), set at 25°C, for 1 minute. The plate was then placed into a SPECTRAmax™ 250 spectrophotometer (set to 30°C) and the absorbance at 350 nm was measured for each sample. This reading served as the blank or reference from which all the other readings at higher temperatures were compared. The assay was initiated by setting heating block 1 to 38°C, programming the temperature cycler to move the microplate to heating block 1, and keeping the microplate there for 3 minutes. Following the equilibration at 38°C, the plate was moved to the 25°C block (Block 4) for 30 seconds, inserted in the spectrophotometer, and absorbance was read at 350 nm. The microplate was then put back into the temperature cycler and was moved to heating block 2, which had been pre-equilibrated at 40° C. After 3 minutes at 40°C, the plate was returned to 25°C (on block 4) for 30 seconds, and was returned to the spectrophotometer for a

measurement of absorbance at 350 nm. This process was repeated 18 more times until the temperature had been raised to 76° C in 2°C increments. After subtraction of the blank absorbance (A_{350} at 25°C), turbidity, reflected in the absorbance value, was plotted as a function of temperature. The thermal denaturation curves for this experiment are shown in Figure 1.